M-I (2) Non-technical abstract. Cystic Fibrosis (CF) is a common, lethal, hereditary disorder caused by mutations of the CF transmembrane conductance regulator (CFTR) gene. The clinical manifestations of CF are primarily in the lung, intestinal tract, pancreas and liver. The respiratory manifestations dominate, with thick mucus, chronic airway infections and inflammation beginning in early childhood and leading to progressive loss of lung function. One of the clinical symptoms of CF is very high concentrations of sweat chloride which occurs as a result of abnormal function of the CFTR gene. The objectives of this protocol are to determine whether administration of Ad_{GV}CFTR.10 (an adenovirus vector carrying the normal cystic fibrosis transmembrane conductance regulator gene) to the skin of cystic fibrosis patients can alter the sweat chloride concentration and/or sweat rate. A total of 15 individuals with a clinically confirmed diagnosis of cystic fibrosis will be studied. They will be split into two groups: Part A (n=7) and B (n=8). The two groups will receive different treatments. Group A will have Ad_{GV}CFTR.10 and vehicle (the solution in which the Ad_{GV}CFTR.10 vector is contained) administration and group B will have Ad_{GV}CFTR.10, Ad_{GV}CD.10 (adenovirus vector expressing the cytosine deaminase gene as a control for CFTR gene), and vehicle administrations. Group B will only be started after group A is finished. In addition to safety and toxicity (which will be evaluated by a variety of safety parameters), the efficacy of the Ad_{GV}CFTR.10 vector will also be determined in this study by assessing the sweat chloride concentration and sweat rate. The skin biopsies at the site of vector administration will allow for the evaluation of persistence of the vector genome and expression of the CFTR mRNA and DNA. At the conclusion of the study, the following objectives will be met: (1) to determine whether intradermal administration of an adenovirus vector containing the cystic fibrosis transmembrane conductance regulator gene to cystic fibrosis patients can alter the sweat chloride concentration and/or sweat rate, and (2) to establish the persistence of the vector genome and expression of CFTR mRNA and DNA as indications of association between their presence and alteration in sweat chloride response and sweat rate.